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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/181,585	10/28/98	RANUM L	110.00900101

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EXAMINER	
SOUAYA, J	
ART UNIT	**PAPER NUMBER**
1655	7

DATE MAILED: 12/23/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

12/23/99

Office Action Summary

Application No.	Applicant(s)
09/181,585	Ranum et al
Examiner	**Group Art Unit**
Jehanne Souaya	1655

☒ Responsive to communication(s) filed on *Oct 28, 1998*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-36* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-36* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Rejections - 35 USC § 112

Enablement

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 4, 10,13, and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting whether an individual is at risk for developing spinocerebellar ataxia type 8 wherein individuals at risk for developing SCA8 have greater than or equal to 80 CTG repeats, does not reasonably provide enablement for determining whether or not an individual has SCA8. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification teaches that the ataxias are a clinically and genetically heterogenous group of neurodegenerative disease that are characterized by trinucleotide repeat expansions, the largest group being that of CAG expansions that are translated into polyglutamine tracts (see p. 1, para. 2). The specification also teaches that in general, a generally high number of CAG repeats

in a particular SCA coding sequence indicates that an individual is suffering from spinocerebellar ataxia, or may develop symptoms in the future, and that the number of CAG repeats that is indicative of spinocerebellar ataxia typically varies with the type of SCA (see p. 2, lines 26-30). The specification teaches that an SCA8 allele with less than 80 CTG repeats is normal, and that an SCA8 allele with less than 91, preferably less than 33 combined CTG and CTA repeats is normal (see p 13, lines 14-23).

The specification lacks guidance to enable one skilled in the art to diagnose ataxia type 8 based on the presence of CTG repeat expansions however. The specification teaches a study of kindreds which include family members exhibiting the symptoms of spinocerebellar ataxia (see p. 32). The specification teaches that 25 clinically affected individuals were identified and that subjects that were homozygous for the SCA8 expansion and their heterozygous siblings were affected to a similar degree (see lines 20-25). However, the specification also teaches that 21 individuals who carried the expanded repeat were not clinically affected at the time of evaluation (see lines 28-31). The specification further teaches that unlike other dominant spinocerebellar ataxias, the age of disease onset for SCA8 does not appear to be significantly correlated with the size of the CTG expansion (see p. 34, lines 24-30).

Indefinite

3. Claims 1-20 and 33 and 34 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite the phrase "complementary oligonucleotides" which is indefinite. It is unclear whether these oligonucleotides are structurally complementary (ie "the complement") or functionally complementary.

Claims 1-20 are indefinite because the claims fail to include a positive process step relating back to the preamble. The preamble states a method for detecting the presence of a DNA fragment located within an at risk allele... but the final process step is analyzing amplified DNA fragment for a repeat region comprising a CTG repeat. This rejection can be overcome by including a final process step relating back to the preamble. Note: the final step should also recite the number of CTG repeats that make SCA8 an "at risk" allele (see section 2 above).

Therefore based on the lack of guidance from the specification and the teaching of unpredictability with regard to *diagnosing* spinocerebellar ataxia type 8 based on the number of repeats, undue experimentation would be required of the skilled artisan to practice the invention as claimed. To be able to diagnose a patient as having spinocerebellar ataxia, the skilled artisan would have to perform a longitudinal kindred analysis, measuring the number of repeats in both affected an unaffected family members, and clinically categorizing each member to determine if an individual who had a large number of repeats actually had or would develop (in the future, hence the need for a longitudinal study) spinocerebellar ataxia.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 21-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Levitan (Textbook of Human Genetics, 3rd ed., 1988, New York., Oxford University Press).

The claims recite "an isolated nucleic acid molecule" which reads on an isolated chromosome. Levitan teaches isolated human chromosome 13, which contains the gene for SCA8. This rejection can be overcome by reciting instead "isolated DNA fragment".

6. Claim 35 is rejected under 35 U.S.C. 102(a) as being anticipated by accession # AL008632, Mistry, S. (Author).

The claim is directed to an isolated oligonucleotide that hybridizes to a repeat region of an isolated SCA8 coding sequence. Accession # AL008632 discloses an oligonucleotide that contains 20 nucleotides exactly complementary to SEQ ID NO 1. Nucleic acid hybridization is dependent on salt concentration, oligonucleotide composition, and temperature. Consequently, a nucleic acid sequence can hybridize to another nucleic acid sequence depending on the reaction

conditions of the hybridization reaction. This rejection can be overcome by reciting instead "an isolated oligonucleotide that specifically hybridizes to a nucleic acid molecule...".

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

Jehanne Souaya
Patent examiner
Dec. 20, 1999